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A Mathematical Algorithm for Dried Blood Spot Quality Assessment and Results concerning Quality from a Newborn Screening Program

Randye Kaye: Hello and welcome to this edition of *JALM* Talk, from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host Randye Kaye.

Newborn screening programs are essential in identifying conditions that can affect a child's long-term health or survival. Newborn screening allows for early detection, diagnosis, and intervention for serious but rare and often treatable conditions. Newborn screening is typically performed from a heel stick blood sample applied to filter paper, known as a dried blood spot. Dried blood spot samples require only a small sample volume and can be easily stored and transported to a laboratory. However, dried blood spots are also prone to pre-analytical errors and laboratories are responsible for establishing their own sample acceptance criteria.

The May 2024 issue of *JALM* features an article describing an optical scanning device and mathematical algorithm that was developed to assess the quality of dried blood spot samples received in a newborn screening laboratory. The authors used the new approach to categorize dried blood spot specimens from 11 maternity wards.

Today, we're joined by the article's first author, Dr. Oana Oprea. Dr. Oprea is the Coordinator of the Emergency Laboratory for the Emergency Clinical County Hospital Targu Mures in Romania and is the Quality Manager for the Clinical Laboratory of the Hospital. Dr. Oprea is also an Assistant Professor in Laboratory Medicine at the George Emil Palade University of Medicine, Pharmacy, Science, and Technology.

Welcome, Dr. Oprea. Firstly, what are some problems that can occur with dried blood spots and how might improper collection affect test results?

Oana Oprea: For example, collection in newborn is especially challenging because they are all so very small and besides that they tend to move when we try to collect the samples. So collection, it's more difficult than in adults. A single drop of blood must

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be obtained and this blood is not usually measured with a volumetric device. It's just a single drop of blood that must be caught in the middle of the circle that is pre-printed on the dry blood spot paper. And so, this is a particular challenge for this type of collection and if the collection is not made properly from a newborn, a range of problems might appear.

If we talk exclusively about newborn screening programs some analytes might have a higher value than in reality and some analytes might have smaller than in reality. In both cases, the wrong medical decision may be taken if the true result is actually higher than the one that we obtained, and then necessarily recollection of the sample will be taken from the newborn and if a smaller value for the analyte is obtained, then we might miss a case because most of the analytes from the national screening programs have a cutoff value and the patient has to be below that value.

Randye Kaye: All right. Thank you. Now, in your article, the article describes an optical scanning device to assess dried blood spot quality. So, can you please tell us more about how that device was developed.

Oana Oprea: So, the device was developed during my PhD studies. I had the help from the engineering department of our university and it started as a mean or a way to evaluate these blood samples by eliminating the human error inherent to this evaluation because when we just look at the blood spot, we sometimes have the illusion that the spot is correctly centered the sample. But it might not be, or in some cases we might think that it's an incorrect sample but the sample is actually correct. So, if we have samples that are not correctly sampled, then we might ask for another sample from the maternity ward.

In our national program, it's a custom that the sample is taken in the day of the discharge of the newborn so it's very difficult to recollect the sample from all newborns that are already have left home. So, we started this device initially by analyzing just some pictures of the blood spot and after that, we realized that we need a device that is more accurate, that has a little bit of speed because it was a very time consuming process.

And we developed the device by using a camera, a simple camera, but inside the device so we don't have the interference from the surrounding light. And after that, we connected this device to a laptop so we can have an incremental notation for the sample. So, we don't waste time by identifying every sample by ourselves.

After that, we started to develop the mathematical algorithms for these kind of devices and for this algorithm we had help from my colleagues from the laboratory.

Randye Kaye: All right, thank you. So, you're talking about the mathematical algorithm. Would you like to expand on how that algorithm works and how it was validated?

Oana Oprea: The first thing I must I think emphasize is that the images are obtained from both sides of the sample. When we perform the samples actually in the laboratory, we tend just to look to the upper side of the dried blood spots where we have the pre-print the sample without looking at the back of the spot. So, we've included for each dry blood spot two images. One from the side A of the spot and one from the side B of the spot. And after that, we compare the size of the two spots on face A and B and how the blood occupies the surface of the pre-printed circle. How it's situated if we take the middle of the pre-printed circle and how it does describes mathematically.

And to develop this algorithm, actually, we use the first set of samples that was evaluated by three members of our laboratory staff and we have started the rules for the mathematical algorithm and another set was used for the validation of the algorithm. So, we make sure that we don't have differences between staff evaluation and algorithm evaluation.

Randye Kaye: All right. Thank you. So, here's another question. The device can detect quality issues after the sample has been collected but how could incorrect blood sampling be prevented?

Oana Oprea: I think by staff training. This is the most important part because we have noticed in our study that in the same maternity wards, the same mistakes are made. So, if we have one type of defect in maternity A, let's say, that defect is the most common in that maternity ward. So probably the staff makes the same mistake every time they collect the samples. So, one way is just to educate the staff and the other, as I can see it for the future maybe, just to have a device that evaluates the samples on the spot. So, when the sample is collected, the nurse just checks if it is a proper collected sample. For hours later, they can do that.

Randye Kaye: So, obviously, training is very important. So, how could the device and the algorithm contribute to staff training for that sample collection?

Oana Oprea: I think if the staff is very aware of the mistakes they do make, because for example, in some maternities, because they could not collect one single drop of blood, they have the tendency to collect more than one drop of blood, and on the same spot,

we had three or four blood spots. So, if the staff is aware of the mistakes, that it's not okay to collect three blood drops instead of just one, maybe they can correct that mistake in the moment of the sampling. I think if they have an immediate answer, is this correct or not correct, they realize what mistake they have done in the moment they collected the first sample.

Randye Kaye: All right. Thank you so much for joining us today.

Oana Oprea: Thank you.

Randye Kaye: That was Dr. Oana Oprea, describing the *JALM* article "A Mathematical Algorithm for Dried Blood Spot Quality Assessment and Results concerning Quality from a Newborn Screening Program."

Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.